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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,051	10/20/2003	Tzc-Bin Chou	529872000110	3492

25225 7590 05/22/2006

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EXAMINER	
JOIKE, MICHELE K	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/690,051	CHOU, TZE-BIN	
	Examiner	Art Unit	
	Michele K. Joike, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *04/23/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Specification

A substitute specification excluding the claims is required pursuant to 37 CFR 1.125(a) because the specification is not in the proper English vernacular. A substitute specification in proper idiomatic English and in compliance with 37 CFR 1.52(a) and (b) is required. The substitute specification filed must be accompanied by a statement that it contains no new matter.

A substitute specification filed under 37 CFR 1.125(a) must only contain subject matter from the original specification and any previously entered amendment under 37 CFR 1.121. If the substitute specification contains additional subject matter not of record, the substitute specification must be filed under 37 CFR 1.125(b) and (c).

Examples of how the instant specification is not in the proper English vernacular are set forth below. Applicant is reminded that these are only examples, and that the specification is replete with grammatical errors.

On page 1, paragraph [0002]:

"However, due to the systematic limitation, the possible living mechanisms are understood mostly through animal models which are composed by manipulated genes."

"The biological mechanism of Drosophila *Melanogaster* has the feature of evolutional conservation."

On page 2, paragraph [0003]:

"In the present time, as the structure genomic projects in model organisms are completed, how to decipher the flood of raw DNA sequences data in understanding gene function in vivo will be one of the major tasks for biology-related researchers."

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988), and the most relevant factors are indicated below:

Nature of the invention. The nature of the invention is a method for making a clipped Drosophila chromosome (cFRT) that is insensitive to a *P* transposase, but remains

sensitive to FLP recombinase. Claims 15-20, specifically, recite the limitation of "further experimentation" (see rejection under 35 USC § 101), therefore the nature of the invention also includes further experimentation.

State of the art. The state of the art is silent regarding the ability to make a clipped Drosophila chromosome that is insensitive to a *P* transposase, but remains sensitive to FLP recombinase. Therefore, the skilled artisan would be forced to rely on the instant specification in order to make and use the claimed invention.

Number of working examples and Guidance provided by applicant. The guidance and working examples set forth in the instant specification are equivalent to the language set forth in the claims. There are many method steps that recite indefinite limitations (see rejections under 112, second paragraph), where it is unclear what is to be performed in order to generate the cFRT. Because it is unclear what steps are to be taken in practicing the method, the skilled artisan cannot make or use the claimed method by relying on the instant specification.

Unpredictability of the art and Amount of experimentation required. The art is highly unpredictable because it is unclear what steps should be performed, what "further examinations" should be performed, etc., in order to practice the method. Because the skilled artisan cannot ascertain this information from either the instant specification or the prior art, the skilled artisan would have to empirically determine these steps, resulting in an undue and unpredictable amount of trial and error experimentation. In fact, a limitation in claims 15-20 indicates that further experimentation is a required

method step. As a result, the skilled artisan cannot make and use the claimed invention, thus the claims are not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are generally indefinite, reciting method steps that are unclear in what is to be performed in order to accomplish the step, or the method as a whole. Each issue of indefiniteness is addressed separately below.

Claim 1 is indefinite because it is unclear if the term "remaining functional to a yeast site-specific flippase recombinase" means that the chromosome encodes a functional recombinase, or if it is "sensitive" to enzymatic action by the recombinase (in the same sense that it is insensitive to the *P* transposase). It would be remedial to exchange the term "functional" with "sensitive." Also, see step (d) of the same claims.

Claim 1 contains the limitation "exposing a *FRT* chromosome to said *P* transposase for occurring a local and imprecise transposition" in step (a) of the claimed methods. This limitation is indefinite because it is unclear if there is antecedent basis for the term "said *P* transposase for occurring a local and imprecise transposition;" this is because it is unclear if the "occurring a local and imprecise transposition" is a characteristic of the transposase, or if it is a separate process step. In addition, it appears as if the term "causing" should replace the term "occurring" in order to bring the

case into proper grammatical standing. If "occurring a local and imprecise transposition" is a process step, it would be remedial to indicate "(a) causing a local and imprecise transposition by exposing an FRT chromosome to said P transposase," etc. If it is a characteristic, there is no antecedent basis for the characteristic.

Claim 1contains the limitation "screening said *P[FRT]* insertion insensitive to said *P* transposase to obtain screened products," which is indefinite because it is unclear what the screening step involves. One might assume that the screening step requires either the presence or the absence the selection marker gene contained in the *P[FRT]* insertion, but it is unknown which (if any) is required in the method. Additionally, it is not even clear if the selection marker is involved in the screening step, the selecting step (i.e., step (c)), neither or both. This further complicates step (c) of the method because it is unclear what is necessary to select "candidate products from said screened products."

Claims 1 and 6 contain the limitation "selecting candidate products from said screened products by further examinations," which is indefinite because it is unclear what process is done (i.e., what are the further examinations) to distinguish candidate products from screened products. In other words, the selection process that is performed in order to arrive at a candidate product while eliminating screened products that are not adequate is unclear, therefore the method step is indefinite. This is because one of skill cannot determine what "further examinations" will discern a "candidate product" from a "screened product."

Claim 1 contains the limitation "exposing said candidate products...and selecting a desired product by said further examinations," which is indefinite because: (a) it is unclear what the candidate product is being exposed to; and (b) it is unclear what a desired product is because it is still unclear what "further examinations" are performed to determine the desirability. The claim is indefinite as it relates to point (a) because the skilled artisan cannot expose the candidate product to an unknown element. The claim is indefinite as it regards point (b) because one cannot determine the "desirability" of a product (which is a relative term) if one does not know what criteria (i.e., the further examinations) are being used to definitively determine when a product is desirable.

Claim 2 recites the limitation "said clipped insertion" in the second line of the claim. There is insufficient antecedent basis for this limitation in the claim. It is indefinite because the skilled artisan cannot determine if the cFRT or the *P[FRT]* insertion is what is examined.

Claims 3 and 5 recite a limitation for examining the "homozygous viability" of a "screened product." This is indefinite because it is unclear how to screen the viability of a non-living biological molecule (i.e., the P[FRT]). Furthermore, it is unclear how this homozygous viability could in anyway represent a genetic background, as recited in claim 5.

Claim 5 recites the limitation "said chromosome's" in the second line of the claim. There is insufficient antecedent basis for this limitation in the claim. It is unclear if the claim is referring to the cFRT or the *FRT* chromosome prior to clipping. It would be remedial to indicate, "said *Drosophila* clipped FRT" or "cFRT" if the former is accurate.

Claim 8 is indefinite because it is unclear if the target sequence is recognized by the *P* transposase, or if it is mutated in such a manner that it is no longer recognized by the *P* transposase. Additionally in claim 8, the following grammatical issues require action: (a) the word "alternated" in line 3 should properly be "altered;" (b) the term "missing of" in sections (1), (2) and (3) is confusing- an alternative is to change it to "a sequence that is missing a..."

Claim 8 is indefinite for the recitation of the phrase "(3) missing of DNA sequences other than those defined in item (1) or item (2)." This skilled artisan cannot know what sequences are included or excluded from this group of sequences, therefore the claim is indefinite for not establishing the metes and bounds of the limitation.

Claim 9 is indefinite because of the phrase "remains the functional activity" in line 2 of the claim. It is unclear if the chromosome represents a functional activity, if the chromosome has a functional activity that it retains, or if it retains the ability to be acted upon in a functional manner.

Claim 10 recites the limitation "derived modification systems thereof," which is indefinite because it is unclear what derivation steps are required to arrive at such a modification system. As such, the skilled artisan cannot reasonably ascertain if a "derived modification system" is being used in the claimed method.

The term "effectiveness" in claims 10 and 11 is a relative term which renders the claim indefinite. The term "effectiveness" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The

skilled artisan cannot reasonably ascertain how to practice the method because the skilled artisan cannot know what is being measured (i.e., what qualifications makes a cFRT effective), or what level of that measurement qualifies as "effective."

Claim 11 recites the phrase "for the description of said cFRT DNA sequences configuration." It is unclear what this term means in the context of the claimed method for generating a *Drosophila* clipped cFRT chromosome that is insensitive to a *P* transposase but remains sensitive to Flp.

Claim 12 recites the phrase "remains to behave normally as a wildtype chromosome feasible of various genetic manipulations." It is unclear what this phrase means, as it does not appear to be in the English vernacular. As such, one cannot reasonably be apprised of what the claim encompasses, therefore it is indefinite because the metes and bounds of the claim have not been defined.

Claim 13 is indefinite because it is unclear how a mutagen or an X-ray can cause the physical movement of a *P[FRT]* from a cFRT chromosome to a different chromosome, and what bearing this has on a method of making the cFRT chromosome.

Claims 13 and 14 recite the term "alternatively," but provide no alternatives. Claim 1, from which the claims depend, is directed to a method of making a chromosome. The terminology set forth in the instant claims suggests that, instead of making the chromosome (as set forth in claim 1), one should "alternatively" do something else instead of performing the elected claimed method (i.e., move an insertion or establish a cell line). Thus, the skilled artisan would not know if the method

steps in claim 1 were necessary to perform the methods of claims 13 and 14, therefore the metes and bounds of the claim are not established.

Claims 15-20 are indefinite because it is unclear where the mutations are generated-in the selection marker, in the FLP sequences, in the *P* transposase sequences, etc. As such, the skilled artisan cannot reasonably be apprised of the metes and bounds of the claims. Furthermore, the purpose of the mutation of the cFRT chromosome (after it has been made) with regard to making the cFRT chromosome (the elected claimed method) is unclear, especially in light of the fact that the claimed method has been completed prior to the mutation of the cFRT. Applicant is reminded that the elected invention is a method of *making* the cFRT, and not a method of using the cFRT.

Claim 18 recites the phrase "can be recovered" in the second line of the claim. This term is indefinite because it is unclear if the step is required to make the chromosome, due to the fact that the phrase "can be" is conditional language (for example, under what conditions would you or would you not "recover"). Therefore, the metes and bounds are not defined because it is unclear if the method step is within the metes and bounds of the claim.

Claim 18 recites the phrase "related bioinformatic manipulation." This term is indefinite because it is unclear how a "bioinformatic manipulation" is determined to be "related" to the method of making a cFRT.

Claim 21 recites the phrase "further analyzed" in the second line of the claim. This term is indefinite because it is unclear what is encompassed by this "further

analysis" (i.e., what step(s) should be performed), therefore the metes and bounds of the term are not defined.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-11 and 13 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,962,804. Although the conflicting claims are not identical, they are not patentably distinct from each other. In Application No: 10/044,423, the parent application of this divisional application, Examiner Lambertson had required restriction between Groups I (claims 1-21) and II (claims 22-28), but later rejoined them and examined claims 1-28. Application No: 10/044,423 was allowed and issued as U.S. Patent No. 6,962,804.

However, before the rejoinder, Applicant had filed this divisional application for claims 1-21. Claims 1-11 and 13 of this application are encompassed by claims 1-11 of U.S. Patent No. 6,962,804.

Specifically, the combination of claims 1 and 3 of the instant application read on claim 1 of U.S. Patent No. 6,962,804. Claims 1 and 3 recite a method for generating a clipped FRT chromosome by exposing the chromosome to a P transposase, and then screening candidate products to determine sensitivity to the transposase, and examining the products for recombination abilities. Claim 1 recites these limitations as well as screening for homozygous viability, and makes more specific references to the chromosomes involved. Claims 2, 4-11 and 13 of the instant application are dependent on claim 1 and read on claims 2-11 of U.S. Patent No. 6,962,804. The claims in the instant application further limit the method to examining the cFRT by PCR, determining the location of the P[FRT], and repeating exposure of the chromosome to P[FRT]. However, P[FRT] can be moved to another chromosome. The cFRT chromosome is the second chromosome and formed due to a target sequence, but remains functional for FLP recombination. Claims 2-11 of U.S. Patent No. 6,962,804 are dependent on claim 1 and drawn to the same subject matter as just described. Claims 12, 14-21 of Application No: 10/044,423 were cancelled during pendency of that application.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele K. Joike, Ph.D. whose telephone number is 571-272-5915. The examiner can normally be reached on M-F, 9:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michele K Joike, Ph.D.
Examiner
Art Unit 1636

DAVID GUZO
PRIMARY EXAMINER